UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/735,099	12/11/2000	Johannes Dapprich	770025.413C1	5343

500 7590 09/14/2006

SEED INTELLECTUAL PROPERTY LAW GROUP PLLC
701 FIFTH AVE
SUITE 6300
SEATTLE, WA 98104-7092

EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 09/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/735,099	DAPPRICH ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *102,105-112 and 115-124* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *102,105-112 and 115-124* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 24 July 2006 has been entered.

Status of the Claims

2. This action is in response to papers filed 24 July 2006 in which claims 102, 109-110, 118-119 and 124 were amended and claims 103-104 and 113-114 were canceled. All of the amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 23 January 2006, not reiterated below, are withdrawn in view of the amendments.

Applicant's arguments have been thoroughly reviewed and are discussed below as they apply to the instant grounds for rejection. New grounds for rejection are discussed.

Claims 102, 105-112, 115-124 are under prosecution.

Priority

Reiterated from previous Office Action

3. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the Provisional Application filed 10 December 1999 upon which priority is claimed, does not provide adequate support under 35 U.S.C. 112 for claims 102-124 of this application. The instant claims are drawn to targeting elements (e.g. primers) that overlap the distinguishing element (e.g. nucleotide of interest). The provisional application does not

provide support for, at least, this element of the instant claims. Therefore, the effective filing date for the instant claims is the filing date of the instant application i.e. 11 December 2000.

Claim Rejections - 35 USC § 112

35 U.S.C. 112: First Paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 102, 105-112, 115-124 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The recitation "characterizing the sites in the genomic DNA molecule of interest that constitute a haplotype" is added to the newly amended independent claim 102 (from which all other claims depend). However, the specification fails to define or provide any disclosure to support such claim recitation. The specification teaches: "In an exemplary embodiment, the method allows for separation of DNA fragments of maternal and paternal origin so that differences between the fragments can be assessed for the determination of a haplotype." (paragraph spanning pages 7-8). However, the specification does not teach sites that constitute a haplotype; and/or characterization of sites; or what is encompassed by site characterization. Therefore, the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

MPEP 2163.06 notes "IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2D 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application." MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*" (emphasis added).

35 U.S.C. 112: Second Paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 102, 105-112, 115-124 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 102, 105-112, 115-124 are indefinite because the claims are drawn to methods of haplotyping. A Haplotype is defined in the art as a set of closely linked alleles that are inherited as a unit e.g. a combination of polymorphisms or alleles. The claims do not define steps for detecting more than one "distinguishing element". The claims merely distinguish a genomic sequence based on a targeting element that overlaps the distinguishing element. Therefore, the instantly claimed method steps cannot be a method of haplotyping based on the meaning of haplotyping as known in the art. Furthermore, while the instant specification discloses the term "haplotyping" the specification does not define the method, as instantly

claimed, as obtaining a haplotype. Therefore, it is unclear whether the method accomplishes the intended haplotyping.

Claims 102, 105-112, 115-124 are further indefinite in Claim 102 for the recitation "the sites" because the recitation lacks proper antecedent basis in the claim. It is suggested the claim be amended to provide proper antecedent basis e.g. replace "sites" with "distinguishing element". It is further noted that "sites" is plural, while the claim recites a singular "distinguishing element".

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 102, 105-111, 115, 117-118 and 122-124 are rejected under 35 U.S.C. 102(b) as being anticipated by Dale et al (U.S. Patent No. 5,856,092, issued 5 January 1999) as defined by Myers ed (Molecular Biology and Biotechnology: A Comprehensive Desk Reference, VCH Publishers, Inc. 1995, page 678).

Regarding Claim 102, Dale et al disclose a method for separating a nucleic acid molecule of interest that differs from another, nearly identical molecule (e.g. allele, Column 17, lines 50-64), the method comprising providing a population of nucleic acid molecules having the molecule of interest and another nearly identical molecule, one strand having a target sequence (i.e. primer complement) and distinguishing element (i.e. distinguishing nucleotide), contacting the molecules with a targeting element i.e. oligonucleotide primer that binds the target sequence and overlaps the distinguishing element (Column 7, lines 8-17), selectively

attaching a separation group in the presence of a polymerase, wherein the separation group comprises an immobilizable and non-terminating nucleotide, wherein the attachment occurs only if the targeting element is bound to the molecule of interest, immobilizing the molecule of interest, removing the molecule from the population of molecules (Column 6, line 48-Column 7, line 35; Column 21, lines15-67; Fig. 2b and Example 2). Dale et al further teach the method wherein target is genomic DNA which is analyzed for multiple nucleotide or base changes (Column 18, lines 50-61) and exemplifies genetic composition of an allelic gene (Column 29-30) Meyers defines "haplotype" as the genetic constitution of an individual based on one member of a pair of allelic genes. Dale et al determines the genetic composition of one an allelic gene and therefore characterizes the genomic DNA that constitutes a haplotype as claimed.

Regarding Claim 105, Dale et al disclose the method wherein the immobilizable non-terminating nucleotides is fluorescein-modified i.e. dNTP-D (Column 4, lines 50-61).

Regarding Claim 106, Dale et al disclose the method wherein the immobilizable and non-terminating nucleotide is a biotinylated NTP (Example 2, Column 25, lines 20-32).

Regarding Claim 107, Dale et al disclose the method wherein the extension product comprises multiple separation groups (Fig. 2b).

Regarding Claim 108, Dale et al disclose the method wherein the extension product is immobilized via multiple separation groups (Example 2 and Fig. 2b).

Regarding Claim 109, Dale et al disclose the method wherein the molecule of interest in topologically attached to the substrate via the extension product (Example 2 and Fig. 2b).

Regarding Claim 110, Dale et al disclose the method further comprising washing the molecule of interest attached to the substrate under high stringency (Fig. 2).

Regarding Claim 111, Dale et al disclose the method wherein the distinguishing element is a heterozygous single nucleotide polymorphism (Column 17, lines 50-64).

Regarding Claim 115, Dale et al disclose the method wherein the substrate is a particle, bead, glass or plastic (i.e. "S S", Column 5, lines 5-8).

Regarding Claim 117, Dale et al disclose the method wherein step (d) i.e. immobilization is performed with relative motion between the oligonucleotide (primer) and substrate (bead) i.e. the reaction mixture containing the extended primer and target is applied to the bead column (Example 2, Column 25, lines 40-44). The step of applying the mixture to the column moves the mixture relative to the column for capture. Absent relative movement between the column and mixture, the complex would not contact the column or be immobilized as illustrated (Fig. 2b).

Regarding Claim 118, Dale et al disclose the method wherein the genomic DNA is denatured (Example 2, e.g. Column 25, line 33).

Regarding Claim 122, Dale et al disclose the method is automated (Column 22, lines 63-67).

Regarding Claim 123, Dale et al disclose the method is miniaturized (a non-specific and relative term) and integrated format (Column 22, lines 63-67)

Regarding Claim 124, Dale et al disclose the method of Claim 102 further comprising a second molecule of interest and target (Column 21, lines 15-Column 22, line 5).

Response to Arguments

10. Applicant argues that Dale et al do not teach step (b) i.e. contacting genomic DNA with a targeting element that distinguishes genomic DNA of a different haplotype. The argument has been considered but is not found persuasive because, as cited above, Dale et al further teach the method wherein target is genomic DNA which is analyzed for multiple nucleotide or base changes (Column 18, lines 50-61) and exemplifies genetic composition of an allelic gene (Column 29-30) Meyers defines "haplotype" as the genetic constitution of an individual based on one member of a pair of allelic genes. Dale et al determines the genetic composition of one an allelic gene and therefore characterizes the genomic DNA that constitutes a haplotype as claimed.

Applicant argues that Dale does not characterize genomic DNA after separation from genomic DNA of a different haplotype. The argument has been considered but is not found persuasive because Table 1, of Dale, clearly illustrates distinguished genomic DNA of different haplotypes.

Applicant argues that Dale does not disclose characterization of haplotypes. The argument has been considered as discussed above i.e. Dale does characterize haplotypes as claimed and as defined in the art. It is noted that the instant claims only require distinguishing a target based on a single "distinguishing element" (step (b)) and based on that distinguishing element haplotyping the DNA. Based on the prior art definition of haplotype and the single element distinction required by the claims, Dale anticipates the instant invention.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claim 112 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dale et al (U.S. Patent No. 5,856,092 issued 5 January 1999) in view of Vary et al (U.S. Patent No. 4,851,331, issued 25 July 1989).

Regarding Claim 112, Dale et al teach the method for separating a nucleic acid molecule of interest that differs from another, nearly identical molecule (e.g. allele, Column 17, lines 50-64), the method comprising providing a population of nucleic acid molecules having the molecule of interest and another nearly identical molecule, one strand having a target

sequence (i.e. primer complement) and distinguishing element (i.e. distinguishing nucleotide), contacting the molecules with a targeting element i.e. oligonucleotide primer that binds the target sequence and overlaps the distinguishing element (Column 7, lines 8-17), selectively attaching a separation group in the presence of a polymerase, wherein the separation group comprises an immobilizable and non-terminating nucleotide, wherein the attachment occurs only if the targeting element is bound to the molecule of interest, immobilizing the molecule of interest, removing the molecule from the population of molecules (Column 6, line 48-Column 7, line 35; Column 21, lines15-67; Fig. 2b and Example 2) wherein the distinguishing element is a heterozygous single nucleotide polymorphism (Column 17, lines 50-64) and wherein the multiple and specific primers are specific for the sequence of interest (e.g. Column 21, lines 19-22) but they are silent regarding the 3' specificity of the primers. However, primers complementary to the sequence of interest at the 3' end of the primers were well known in the art at the time the claimed invention was made as taught by Vary et al (Fig. 4). Vary et al teach a method similar to that of Dale wherein primers are specifically extended based on complementation at the 3' end (Fig. 4). Vary et al teach that this 3' end complementation prevents extension of mismatched primers and is the preferred primer for extending and detecting only the sequence of interest (Column 2, line 60-Column 3, line 43). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the 3' specific primers of Vary et al to the sequence-specific primer extension of Dale et al. One of ordinary skill in the art would have been motivated to do so for the expected benefit of extending and detecting only the sequence of interest as desired in the art (Vary, Column 2, line 60-Column 3, line 43).

Response to Arguments

13. Applicant asserts that Vary et al do not cure the deficiencies of Dale et al. The argument has been considered but is not found persuasive because, as stated above, Dale is not found deficient.

Applicant further asserts that sufficient motivation has not been provided for the combination because the combination would complicate the method of Dale because the sequence-specific detection of Dale would be sufficient. The argument has been considered but is not found persuasive because as stated above, Vary et al teaches the primer extension confirms 3' complementation and detection of sequence of interest. Hence, one would have been motivated to obtain that confirmation.

14. Claim 116 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dale et al (U.S. Patent No. 5,856,092 issued 5 January 1999) in view of Zhou et al (U.S. Patent No. 6,355,491, filed 17 September 1999).

Regarding Claim 116, Dale et al disclose a method for separating a nucleic acid molecule of interest that differs from another, nearly identical molecule (e.g. allele, Column 17, lines 50-64) wherein the immobilizing the substrate is a particle or bead (i.e. "S S", Column 5, lines 5-8 and Fig. 2b) but they are silent regarding cleavable linkage of the separation group. However, cleavable linkers were well known in the art at the time the claimed invention was made as taught by Zhou et al (Column 16, line 60-Column 17, line 33). Zhou et al teach that the cleavable linker provides for removal of the beads following immobilization of the target (Column 17, lines 28-33). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the cleavable linker of Zhou et al to the separation group of Dale et al. One of ordinary skill in the art would have been motivated to do so for the expected benefit of bead removal following target immobilization as desired in the art (Zhou et al, Column 17, lines 28-33).

Response to Arguments

15. Applicant asserts that Zhou et al do not cure the deficiencies of Dale et al. The argument has been considered but is not found persuasive because, as stated above, Dale is not found deficient.

16. Claims 119-120 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dale et al (U.S. Patent No. 5,856,092 issued 5 January 1999) in view of Radding et al (U.S. Patent No. 4,888,274, issued 19 December 1989).

Regarding Claims 119-120, Dale et al disclose a method for separating a nucleic acid molecule of interest that differs from another, nearly identical molecule (e.g. allele, Column 17, lines 50-64), the method comprising providing a population of nucleic acid molecules having the molecule of interest and another nearly identical molecule, one strand having a target sequence (i.e. primer complement) and distinguishing element (i.e. distinguishing nucleotide), contacting the molecules with a targeting element i.e. oligonucleotide primer that binds the target sequence and overlaps the distinguishing element (Column 7, lines 8-17), selectively attaching a separation group in the presence of a polymerase, wherein the separation group comprises an immobilizable and non-terminating nucleotide, wherein the attachment occurs only if the targeting element is bound to the molecule of interest, immobilizing the molecule of interest, removing the molecule from the population of molecules (Column 6, line 48-Column 7, line 35; Column 21, lines15-67; Fig. 2b and Example 2) wherein the separation uses known binding pairs e.g. antibody/antigen (Column 16) but they are silent regarding DNA binding proteins or RecA.

However, DNA-binding protein (i.e. RecA) stabilization of hybrid nucleic acids was well known in the art at the time the claimed invention was made as taught by Radding et al who

teaches that RecA facilitates formation of a specific and stable duplex and provides for enrichment of target DNA (Abstract). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to add the RecA of Radding to the duplex formation of Dale et al for the expected benefit of facilitating specific and stable duplex formation and target DNA enrichment as taught by Radding (Abstract).

Response to Arguments

17. Applicant asserts that Radding et al do not cure the deficiencies of Dale et al. The argument has been considered but is not found persuasive because, as stated above, Dale is not found deficient.

18. Claim 121 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dale et al (U.S. Patent No. 5,856,092 issued 5 January 1999) in view of Leob (U.S. Patent No. 5,654,148, issued 5 August 1997).

Regarding Claim 121, Dale et al teach the method of Claim 1 wherein the target detection diagnosis various genetic conditions (Column 17, lines 50-64) but they are silent regarding the size (kb) of the target. However, targets of 100kb (e.g. total DNA) were well known in the art of genetic diagnosis and haplotyping as taught by Loeb (Column 8, line 10-Column 9, lien 46) whereby chromosomal haplotypes, especially those associated with disease, are identified (Column 9, lines 1-13). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the targets of Loeb to the genetic detection methods of Dale et al. One of ordinary skill in the art would have been motivated to do so for the expected benefit of identifying disease-associated haplotypes as taught by Loeb (Column 19, lines 1-13).

Response to Arguments

19. Applicant asserts that Vary et al do not cure the deficiencies of Dale et al. The argument has been considered but is not found persuasive because, as stated above, Dale is not found deficient.

Conclusion

20. No claim is allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

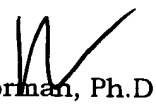
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
September 8, 2006